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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,634	04/01/2004	Tania Kastelic	608352000100	8704

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EXAMINER	
QIAN, CELINE X	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/814,634	KASTELIC ET AL.	
	Examiner	Art Unit	
	Celine X. Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,10,13-15 and 23-39* is/are pending in the application.

4a) Of the above claim(s) *10,13 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,15 and 23-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Claims 9, 10, 13-15, 23-39 are pending in the application.

Election/Restrictions

Applicant's election without traverse of Group II in the reply filed on 9/14/06 is acknowledged.

Accordingly, claims 10, 13 and 14 are withdrawn from consideration for being directed to non-elected subject matter. Claims 9, 15, 23-29 are currently under examination.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821(d) because the Application contains references to sequences in the specification that fail to recite a "SEQ ID NO." The sequences disclosed in the drawings lack sequence identifier. The above reasons are set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-

filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 09/869,159, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Claims 28 and 35 recites "CRD" which is not disclosed in 'application. As such, the priority for claims directing to "CRD" is the filing date of the instant application 4/1/04.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9, 24-27, 29 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Zubiaga et al. (1995, MCB, Vol 15, No.4, pages 2219-2230).

The claims are drawn to a transfected cell line comprising an expression cassette consisting of one or more genes encoding a protein having a detectable signal and 5' and 3' UTR sequences comprising operably-linked expression control elements; and 2) an instability region consisting of at least 10-1500 nucleotides of the 3'UTR of a gene sequence which confers instability to a mRNA, and wherein the instability region is heterologous to the 3' UTR sequence; and a control expression system which does not have the mRNA instability sequence.

The claims are also drawn to said expression system, wherein the instability region is from genes coding for cytokines, chemokines, GM-CSF, *c-fos*, etc.

Zubiaga et al. disclose an expression vector comprising *c-fos* promoter operatively linked to globin gene, wherein several ARE isolated from *c-fos* is inserted into 3'UTR of the globin gene (see page 2220, 2nd col., 6th paragraph), resulting in sets of cell lines comprises different expression constructs. Zubiaga et al. also disclose that a control plasmid pRSV-lacZ, comprising a gene coding for expression of lacZ, 5'and 3'UTR for expression of said gene without mRNA instability sequence (see page 2221, 1st col., 2nd paragraph, lines 4-9). Zubiaga et al. further disclose that these construct are co-transfected into NIH-3T3 cells (see page 2221, 1st col., 2nd paragraph, lines 1-4). Therefore, Zubiaga et al. disclose the instantly claimed inventions.

Claims 30-34, 36, 37 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Banholzer et al (Molecular Cellular Biology, 1997, Vol 17, No.6, pages 3254-3260).

The claims are drawn to a set of cell lines wherein the 1st cell line comprises an expression cassette consisting of one or more genes encoding a protein having a detectable signal and 5' and 3' UTR sequences comprising operably-linked expression control elements; and 2) an instability region consisting of at least 10-1500 nucleotides of the 3'UTR of a gene sequence which confers instability to a mRNA, and wherein the instability region is heterologous to the 3' UTR sequence; and a second cell line comprises a control expression system which does not have the mRNA instability sequence. The claims are further drawn to a set of cell lines as recited above, wherein the instability region is from genes coding for cytokines, chemokines, GM-CSF, *c-fos*, etc. or wherein at least one cell line is stably transfected. The claims are also drawn to an expression system comprising the cell lines and a test compound.

Banholzer et al. disclose that rapamycin promotes degradation of IL-3 transcripts at posttranscriptional level via 3' UTR (see page 3257, 2nd col., 1st paragraph). Banholzer et al. disclose two cell lines stably transfected with IL-3 expression system either with (VD1-M1) or without (VD1-M1ΔAU) mRNA instability sequence (3' UTR) (see page 3256, 1st col., lines 1-3). Banholzer et al. also disclose that following rapamycin and FK506 treatment, endogenous and exogenous wild type IL-3 decayed with very similar kinetics (see Figure 3b, left panel) whereas the exogenous mutant IL-3 mRNA level is not affected by either compound (Figure 3b, right panel, and 3c). The method and assay system disclosed by Banholzer et al. identifies rapamycin and FK506 as compounds that induce mRNA degradation. Therefore, Banholzer et al. disclose the instant claimed inventions.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zubiaga et al., in view of Banholzer et al.

The teaching of Zubiaga and Banholzer were discussed above.

Regarding claims 15 and 23, Zubiaga et al. do not teach an assay system for screening compounds which destabilize mRNA that comprises a cell line as claimed in claim 9 and a test compound. And wherein the cell line is stably transfected.

It would have been obvious for one of ordinary skill in the art to develop an assay system as taught by Banholzer that is able to screen compounds such as rapalogs for their ability to modulating the mRNA instability sequence. Based on the teaching of Zubiaga, the ordinary skilled in the would have been motivated to screening compounds that would affect ARE sequence instability using the heterologous expression construct as disclosed in Zubiaga et al. One of ordinary skill in the art would also be motivated to use stably transfected cell lines because they are easy to maintain such that one does not have to do transfection every time to test a compound. The level of skill in the art is high. Absent evidence from the contrary, one of ordinary skilled in the art would have reasonable expectation of success to use the cell line taught by Zubiaga as a system to test compounds and make the cell line a stably transfected cell for said purpose. Therefore, the claimed invention would have been *prima facie* obvious at the time the invention was made.

Claims 28 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zubiaga et al., in view of Lemm and Ross (Molecular and Cellular Biology, 2002, Vol 22, No.12, pages 3959-3969).

The teaching of Zubiaga and Banholzer were discussed above. However, neither references teaches a coding region instability determinant as the instability sequence.

Lemm and Ross teach a 249 nucleotide coding region from c-myc destabilizes c-myc mRNA. Lemm and Ross also teach that said nucleotide sequence destabilizes beta-globin mRNA when inserted in frame within the coding region of said beta-globin gene (see page 3959, 2nd col., 2nd paragraph).

It would have been obvious to one of ordinary skill in the art to use the cell lines with constructs that have instability sequence as taught by either Zubiaga et al. or Banholzer et al. to test compounds that affect coding region instability determinants (CRD) from c-myc. One of ordinary skill in the art would have been motivated to do so for screening compounds that modulates the activity of the CRD. Absent evidence from the contrary, the ordinary artisan would have reasonable expectation of success to insert the CRD into a construct which can then be transfected into a cell line for testing compounds. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 15, 23-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 9 and 30, the recitation of "a second DNA sequence corresponding to one or more mRNA instability sequence derived from..." renders the claim indefinite because it

is unclear what constitutes the scope of "corresponding to." Does it mean the DNA share certain homology or comprises the mRNA instability sequence? The term "derived" also renders the claims indefinite because the nature and number of derivative process is unknown. As such, the metes and bounds of the claim cannot be established. Claims 15, 23-39 are also rejected for comprising said terms or their dependency to claims 9 and 30.

Regarding claim 38, the recitation of "wherein said heterologous instability sequence in said transfected cell line comprising a DNA expression vector is inserted into said 3'UTR sequence" renders the claim indefinite because it is unclear whether it is the instability sequence of the expression vector is inserted into said 3' UTR.

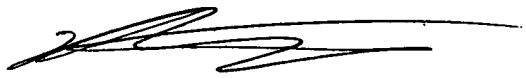
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELINE QIAN, PH.D.
PRIMARY EXAMINER



Notice to Comply	Application No.	Applicant(s)	
	10/814,634	Kestelic et al.	
	Examiner	Art Unit	
	Celine Qian	1636	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: The sequences in Figure and specification lack sequence identifier.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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